

0420 2459-1-003CIP #9

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT:

Zhou, Ming-Ming et al.

SERIAL NO.:

09/784,553

EXAMINER:

Not Yet Assigned

FILED:

February 16, 2001

ART UNIT

Not Yet Assigned

FOR

METHODS OF IDENTIFYING MODULATORS OF

BROMODOMAINS

CERTIFICATE OF MAILING UNDER 37 CFR 1.8

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage in an envelope addressed to the ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON, DC 20231 on April 7, 2003.

Anne M. Jones

(Name of Person Depositing Mail)

(Signature and Dat

PRELIMINARY AMENDMENT

ASSISTANT COMMISSIONER FOR PATENTS WASHINGTON, D.C. 20231

Dear Sir:

Please enter the following amendments into the present application.

IN THE DRAWINGS:

Please delete Figure 13-1 through 13-13 without prejudice or disclaimer.

IN THE SPECIFICATION:

Please substitute the following amended paragraph for the paragraph on page 10, lines 19-25:

In a preferred embodiment the compound is selected by performing rational drug design with the set of atomic coordinates obtained from one or more of Tables 1-5 and 10-14. More preferably the selection is performed in conjunction with computer modeling. Compounds selected by these methods are also part of the present invention. Preferably the compound is a small organic molecule. More preferably the compound is an analog of acetyl-lysine. Even more preferably, the compound is not included in Table 15-1 to 15-33.

Please substitute the following amended paragraph for the paragraph starting on page 10, line 25 and ending on page 11, line 19:

The present invention also provides methods of identifying a compound that modulates the stability of the binding complex formed between P/CAF and Tat that is acetylated at the lysine residue at position 50 of SEQ ID NO:45. In one such embodiment the method comprises contacting the bromodomain of P/CAF or a fragment thereof with a binding partner in the presence of the compound under conditions in which the bromodomain of P/CAF and the binding partner bind in the absence of the compound. The stability of the bromodomain of P/CAF and the binding partner is then determined (e.g., measured). When there is a change in the stability of the binding complex between the bromodomain of P/CAF and the binding partner in the presence of the compound, the compound is identified as a modulator. In one embodiment of this type the binding partner is Tat that is acetylated at the lysine residue at position 50 of SEQ ID NO:45. In a preferred embodiment the binding partner is a fragment of Tat comprising an acetyl-lysine at position 50. In still another embodiment the binding partner is an analog of the fragment of Tat comprising an acetyl-lysine at position 50. When the stability of the bromodomain of P/CAF for the binding partner increases in the presence of the compound, the compound is identified as a stabilizing agent, whereas when the stability of the bromodomain of P/CAF for the binding partner decreases in the presence of the compound, the compound is identified as an inhibitor of the Tat-P/CAF complex. In a preferred embodiment the compound is selected by performing rational drug design with the set of atomic coordinates obtained from one or more of Tables 1-5 and 10-14. More preferably the selection is performed in conjunction with computer modeling. Compounds identified by these methods are also part of the present invention. Preferably the compound is an analog of acetyl-lysine. More preferably the compound is a small organic molecule not included in Table 15-1 to 15-33.

Please substitute the following amended paragraph for the paragraph starting on page 11, line 27 and ending on page 12, line 2:

Another aspect of the present invention provides methods of preventing, and/or retarding the progression and/or treating HIV infection in an individual. One such method employs administering to the individual compounds that modulate the Tat-P/CAF complex selected by performing rational drug design with the set of atomic coordinates obtained from one or more of Tables 1-5 and 10-14. In a preferred embodiment the compound administered is an acetyl-lysine

analog. In a particular embodiment this compound is a small organic molecule contained in Table 15-1 to 15-33. Preferably the compound either de-stabilizes or inhibits the Tat-P/CAF complex.

Please substitute the following amended paragraph for the paragraph on page 16, line 19 through line 24:

Figure 12 depicts the chemical structure common to the acetyl-lysine analogs of the present invention. R_1 , R_2 , and R_3 can be H, CH_3 , a halogen (*e.g.*, F, Cl, Br, I etc.), OH, SH, or NH_3^+ . R4 can be an alkyl (including a peptide/protein attached thereto such as a peptide comprising an acetyl-lysine in which the "N" of the structure depicted is the epsilon nitrogen (*i.e.*, N^{e}) of a lysyl residue), or an aryl group. *See also* Table 15-1 to 15-33 for examples.

Please delete line 26 on page 16.

Please substitute the following amended paragraph for the paragraph on page 20, line 11 through line 25:

The present invention provides the first detailed structural information regarding a bromodomain and a bromodomain complexed with its acetylated binding partner. The present invention therefore provides the three-dimensional structure of the bromodomain and a bromodomain acetylated binding partner complex. Since the interaction of the bromodomain with a histone for example, can play a significant role in chromatin remodeling/regulation, the structural information provided herein can be employed in methods of identifying drugs that can modulate basic cell processes by modulating the transcription. In a particular embodiment, the three-dimensional structural information is used in the design of a small organic molecule for the treatment of cancer or as disclosed below, HIV-1 infection and/or AIDs. In addition, the present invention provides a critical structural feature for a class of inhibitors (acetyl-lysine analogs) of the interaction between bromodomains and their protein binding partners which contain an acetylated-lysine (*e.g.*, Tat with P/CAF), *see* Figure 12, as well as a compilation of compounds that share this critical feature, *see* Table 15-1 to 15-33.

Please substitute the following amended paragraph for the paragraph on page 24, line 25 through line 28:

As used herein the term "acetyl-lysine analog" is used interchangeably with the term "analog of acetyl-lysine" and is a compound that contains the acetyl-amine-like structure as depicted in Figure 12. Examples of acetyl-lysine analogs are included in Table 15-1 to 15-33.

Please substitute the following amended paragraph for the paragraph on page 44, line 11 through line 17:

Initially a potential drug could be obtained by screening a random peptide library produced by recombinant bacteriophage for example, [Scott and Smith, *Science*, **249**:386-390 (1990); Cwirla *et al.*, *Proc. Natl. Acad. Sci.*, **87**:6378-6382 (1990); Devlin *et al.*, *Science*, **249**:404-406 (1990)] or a chemical library. In particular, based on the NMR structural analysis provided herein, compounds that comprise an "acetyl-amine-like" structure as depicted in Figure 12 are particularly good candidates. Examples of such "acetyl-lysine analogs" are included in Table 15-1 to 15-33.

Please substitute the following amended paragraph for the paragraph starting on page 55, line 28, through line 4 on page 56:

According to the invention, the component or components of a therapeutic composition, *e.g.*, an agent of the invention that interferes with the bromodomain-acetyl-lysine binding complex such as the peptide having the amino acid sequence of SEQ ID NOs:4, 5, 6, 46, or 47, or an acetyl-lysine analog as defined by Figure 12 and exemplified in Table 15-1 to 15-33, and a pharmaceutically acceptable carrier, may be introduced parenterally, transmucosally, *e.g.*, orally, nasally, or rectally, or transdermally. Preferably, administration is parenteral, *e.g.*, via intravenous injection, and also including, but is not limited to, intra-arteriole, intramuscular, intradermal, subcutaneous, intraperitoneal, intraventricular, and intracranial administration.

Please insert Table 15-1 to 15-33, attached hereto as Table 15-1 through 15-33, into the specification after page 83 and before the claims.

IN THE CLAIMS:

Please cancel claims 37 through 43 without prejudice or disclaimer.

2459-1-003CIP

Please substitute the following amended claims for the original claims having the same claim number:

- 29. (Amended) A compound that is a small organic molecule identified by the method of Claim 28; wherein said compound is an analog of acetyl-lysine, but with the proviso that the compound is not included in Table 15-1 to 15-33.
- 34. (Amended) A compound that is a small organic molecule identified by the method of Claim 33; wherein said compound is an analog of acetyl-lysine, but with the proviso that the compound is not included in Table 15-1 to 15-33.
- 35. (Amended) An agent that can modulate the binding of P/CAF and Tat; wherein said agent is an analog of acetyl-lysine, but with the proviso that the agent is not included in Table 15-1 to 15-33.

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REMARKS

Claims 1-43 are pending. Claims 37-43 have been cancelled without prejudice or disclaimer. Claims 29, 34 and 35 have been amended. Thus, claims 1-36 remain under consideration.

The amendments to the specification and claims were rendered to clarify aspects of the invention. Table 15-1 to 15-33 presents identical data to that originally included in Figure 13, which has now, accordingly, been deleted. No New Matter has been added by way of these amendments.

A Petition for Correction of Inventorship is attached herein in accordance with 1.48(b). This correction is respectfully requested in light of the claims cancelled by way of this amendment.

Attached hereto is a marked-up version of the changes made to the specification and the claims by the current amendment. The attachment is captioned "Version with markings to show changes made."

Conclusion

Examination on the merits is respectfully requested.

Respectfully submitted,

Veronica Mallon, Ph.D. Agent for Applicants

erorica mallon

Registration No. 52,491

KLAUBER & JACKSON 411 Hackensack Avenue Hackensack, New Jersey 07601

Date: April 7, 2003

Attachment: Table 15-1 to 15-33

Petition for Correction of Inventorship

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The following amended paragraph will replace the original paragraph on page 10, lines 19-25:

In a preferred embodiment the compound is selected by performing rational drug design with the set of atomic coordinates obtained from one or more of Tables 1-5 and 10-14. More preferably the selection is performed in conjunction with computer modeling. Compounds selected by these methods are also part of the present invention. Preferably the compound is a small organic molecule. More preferably the compound is an analog of acetyl-lysine. Even more preferably, the compound is not included in [Figure 13] <u>Table 15-1 to 15-33</u>.

The following amended paragraph will replace the original paragraph starting on page 10, line 25 and ending on page 11, line 19:

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is selected by performing rational drug design with the set of atomic coordinates obtained from one or more of Tables 1-5 and 10-14. More preferably the selection is performed in conjunction with computer modeling. Compounds identified by these methods are also part of the present invention. Preferably the compound is an analog of acetyl-lysine. More preferably the compound is a small organic molecule not included in [Figure 13] <u>Table 15-1 to 15-33</u>.

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Line 26 on page 16 has been deleted:

[Figure 13 depicts examples of acetyl-lysine analogs. [PRIOR ART]]

The following amended paragraph will replace the original paragraph on page 20, line 11 through line 25:

The present invention provides the first detailed structural information regarding a bromodomain and a bromodomain complexed with its acetylated binding partner. The present

invention therefore provides the three-dimensional structure of the bromodomain and a bromodomain acetylated binding partner complex. Since the interaction of the bromodomain with a histone for example, can play a significant role in chromatin remodeling/regulation, the structural information provided herein can be employed in methods of identifying drugs that can modulate basic cell processes by modulating the transcription. In a particular embodiment, the three-dimensional structural information is used in the design of a small organic molecule for the treatment of cancer or as disclosed below, HIV-1 infection and/or AIDs. In addition, the present invention provides a critical structural feature for a class of inhibitors (acetyl-lysine analogs) of the interaction between bromodomains and their protein binding partners which contain an acetylated-lysine (e.g., Tat with P/CAF), see Figure 12, as well as a compilation of compounds that share this critical feature, see [Figure 13] Table 15-1 to 15-33.

The following amended paragraph will replace the original paragraph on page 24, line 25 through line 28:

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The following amended paragraph will replace the original the paragraph on page 44, line 11 through line 17:

Initially a potential drug could be obtained by screening a random peptide library produced by recombinant bacteriophage for example, [Scott and Smith, Science, 249:386-390 (1990); Cwirla et al., Proc. Natl. Acad. Sci., 87:6378-6382 (1990); Devlin et al., Science, 249:404-406 (1990)] or a chemical library. In particular, based on the NMR structural analysis provided herein, compounds that comprise an "acetyl-amine-like" structure as depicted in Figure 12 are particularly good candidates. Examples of such "acetyl-lysine analogs" are included in [Figure 13] Table 15-1 to 15-33.

The following amended paragraph will replace the original paragraph starting on page 55, line 28, through line 4 on page 56:

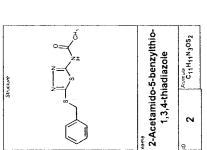
According to the invention, the component or components of a therapeutic composition, *e.g.*, an agent of the invention that interferes with the bromodomain-acetyl-lysine binding complex such as the peptide having the amino acid sequence of SEQ ID NOs:4, 5, 6, 46, or 47, or an acetyl-lysine analog as defined by Figure 12 and exemplified in [Figure 13] <u>Table 15-1 to 15-33</u>, and a pharmaceutically acceptable carrier, may be introduced parenterally, transmucosally, *e.g.*, orally, nasally, or rectally, or transdermally. Preferably, administration is parenteral, *e.g.*, via intravenous injection, and also including, but is not limited to, intra-arteriole, intramuscular, intradermal, subcutaneous, intraperitoneal, intraventricular, and intracranial administration.

IN THE CLAIMS:

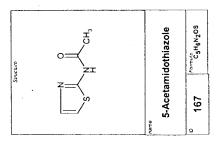
The following claims have been amended to replace the original claims having the same claim number:

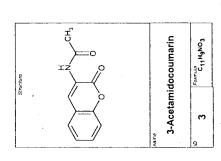
- 29. (Amended) A compound that is a small organic molecule identified by the method of Claim 28; wherein said compound is an analog of acetyl-lysine, but with the proviso that the compound is not included in [Figure 13] <u>Table 15-1 to 15-33</u>.
- 34. (Amended) A compound that is a small organic molecule identified by the method of Claim 33; wherein said compound is an analog of acetyl-lysine, but with the proviso that the compound is not included in [Figure 13] <u>Table 15-1 to 15-33</u>.
- 35. (Amended) An agent that can modulate the binding of P/CAF and Tat; wherein said agent is an analog of acetyl-lysine, but with the proviso that the agent is not included in [Figure 13] <u>Table 15-1 to 15-33</u>.

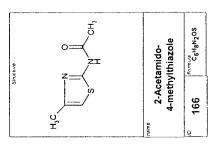




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Sinclure		name Melatonin	31





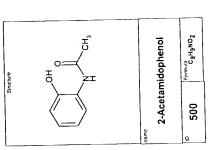


thre	±° z-√	lcytosine	Formula CeH7N3O2
Sincure	Ĭ ZI	name N4-Acetylcytosine	277

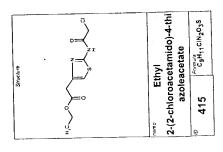
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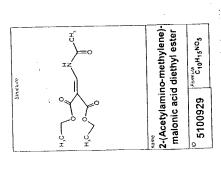
TABLE 15 - 1

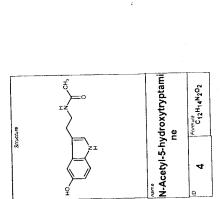


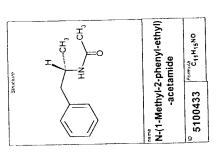


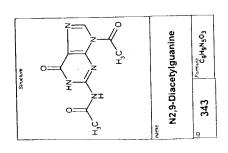
Spreium O	N-(2-(3,4-Dimethoxy-phenyl)-ethyl)-acetamide	⁵ 5102090 Formula 5102090
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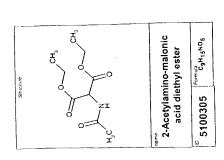
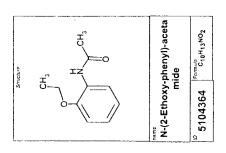
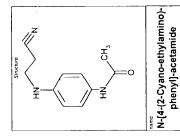


TABLE 15 - 2

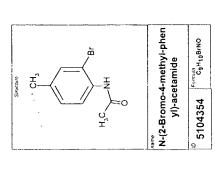


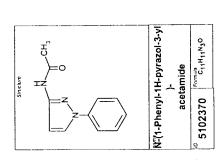
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N N N N N N N N N N N N N N N N N N N	777	D 5102701 Formula C11H12N402

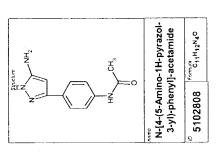


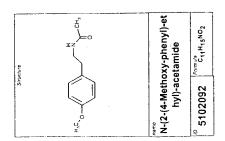


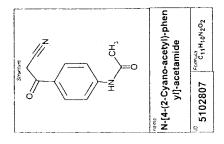
5102700 Formula 11113N30





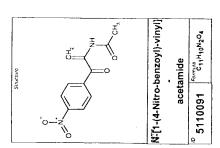


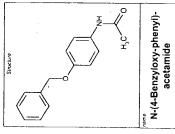




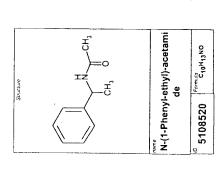


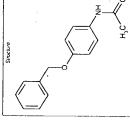
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	N-(3-Cyano-4 ro-benzo[b]tl aceta	5107418

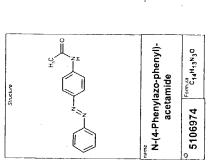


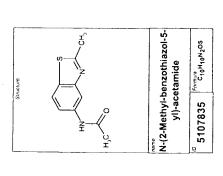


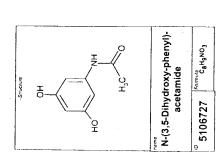
5107131 Formula 5107131

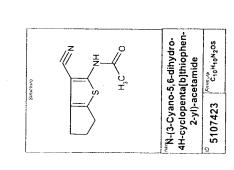






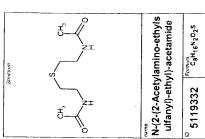


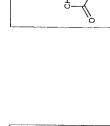


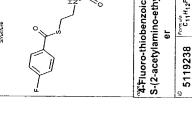


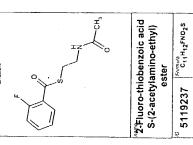


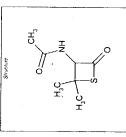
,	
Sirveiure	4-Fluoro-thiobenzoic acid

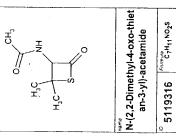


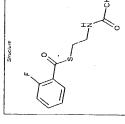


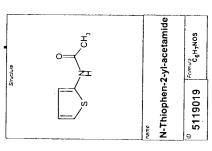


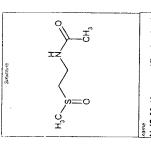




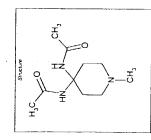








TZ O T	กษาย N-(2-Methanesulfinyl-ethyl)- acetamide ¹⁰ 5119302 ^{Formula}
ν=0 υ π	Nore N-(2-Methane acet:



N-(4-Acetylamino-1-methyl-piperidin-4-yl)-acetamide

5118841 Formula C10H19N3O2

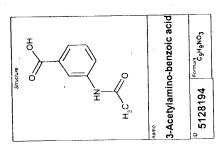
•			
Smature	O=\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	سهر (2-Methylsulfanyl-ethyl)-a cetamide	Formula C5H11NOS
rs.	SO D S S S S S S S S S S S S S S S S S S	N-(2-Methylsu ceta	² 5119299

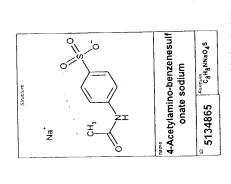
TABLE 15 - 5

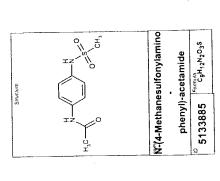
۱ 4	2003	CA2 30%
A	EMAKK	

Sincina	Z V H H O	N-(5-Methyl-benzo[1,2,5]thi adiazol-4-yl)-acetamide	5131057 Formula 49N3OS

	(Z)-3-(4-Acetylamino-pheny Icarbamoyl)-acrylic acid 5135478
--	---



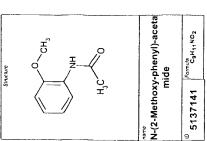


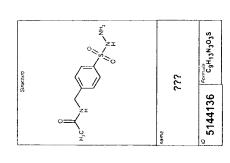


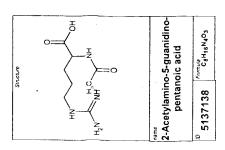
Simetime CH,	(4"Acetylamino-phenyl)-eth yl-dimethyl-ammonium chloride	5132286 Formula 5132286

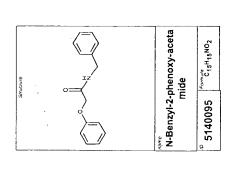


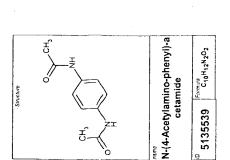


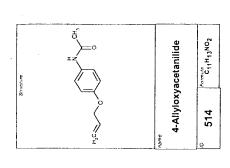


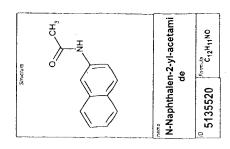












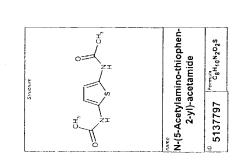
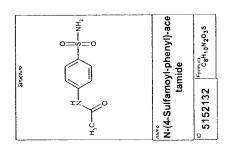
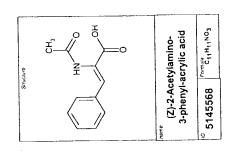


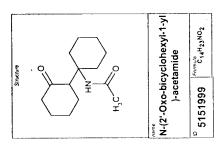
TABLE 15 - 7

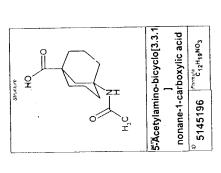


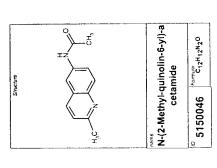


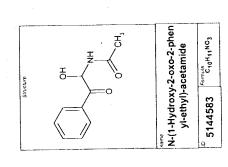












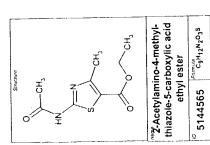
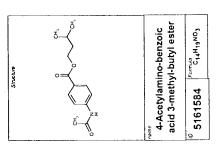
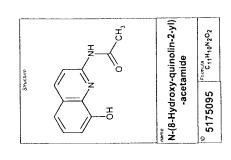


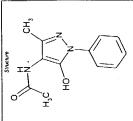
TABLE 15 - 8











N°(5-Hydroxy-3-methyl-1-p henyl-1H-pyrazol-4-yl)-acet amide

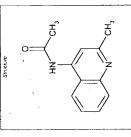
2-Chloro-N-(2-hydroxy-5-nit ro-benzyl)-acetamide

%-(4,5,6,7-Tetrahydro-benz o[b]thiophen-2-yl)-acetamid

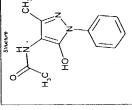
5156862 Formula 13NOS

5157409 Formula CIN204

5160581 Formula C12H13N3O2

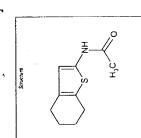


5170552 Formula 12N20



र्स्	midaz
IZ O	2-Acetylamino-3-(3H-imidaz
S N	tylamin
	2-Ace

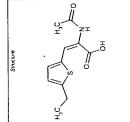
IZ O	2-Acetylamino-3-(3H-imidaz ol-4-yl)-propionic acid	Formula CaH11N3O3
Of The Control of the	2-Acetylamin ol-4-yl)-pro	5163605



arri):	O TZ	en-9-yl)-acetam ide	Formula C15H13NO2
Structure		nane N-(9H-Xanthen-9-yl)-acetam ide	5161930

Sinceture CH,
--

Structure	LO Z	H ₃ C M-[4-(2,5-Dimethyl-pyrrol-1-yl)-phenyl]-acetamide	Formula C14H16N2O
Sirv	J. F.	H ₃ C mm (12,5-Dim)	5210476



(E)-2-Acetylamino-3-(5-ethy I-thiophen-2-yl)-acrylic acid Formula C11H13NO3S 5190720

N-(5-Oxo-1-phenyl-4,5-dihy dro-1H-pyrazol-3-yl)-acetamide 5192544 Formula C11H11N302

N-(5-Propionyl-thiophen-2-yl)-acetamide Formula C9H11NO2S 5190716

N-(4-Phenoxy-phenyl)-acet amide 5191921 Framula C14H13NO2

Clareto	O ZI	
L	 Ľ.	

	-	1	
Smeture	40 40 40 40	سو 3-Acetylamino-nonanoic acid	5190776 Formula C111H21NO3
	— °	3-A	5.

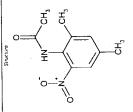


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REAL TRANSPORTER	e

3/	j	
	H,CO.	۸-(4-Ethoxy-3-nitro-phenyl) -acetamide

C10H12N2O4	
5211946	

Structure	₹— ⟨	CH ₃	N-[2-(1-Methyl-cyclopropyl) -phenyl]-acetamide	Formula C12H15NO
Strut	ı,	`o	N-[2-(1-Methy -phenyl]-a	5216286



N-(2,4-Dimethyl-6-nitro-phe

nyl)-acetamide

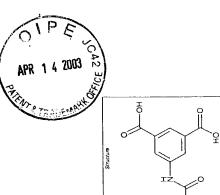
N-(4-Hydroxymethanesulfo nyl-phenyl)-acetamide

1-methyl-ethyl}-acetamide N-{1-{5-[(Z)-Hydroxyimino}-4-methyl-cyclohex-3-enyl}-Formula C12H20N2O2 5213911

(4-acetylamino-phenyl)-ami

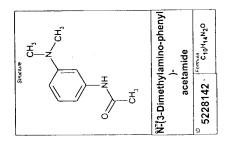
"Furan-2-carboxylic acid

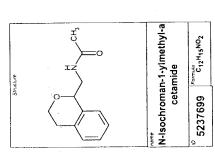
N°(3-Chloro-1,4-dioxo-1,4-di hydro-naphthalen-2-yl)-Formula C12HgCINO3 acetamide 5212521

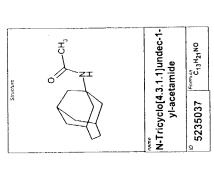


Structure	10	OH OH	مسر 5-Acetylamino-isophthalic acid	6233529 Formula C10HgNO5

Seneture O CH ₃ N-(3-Oxo-3-phenyl-propion yl)-acetamide 5238359				,
	Sinchio	₹	N-(3-Oxo-3-phenyl-propion yl)-acetamide	l

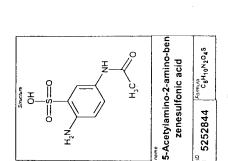


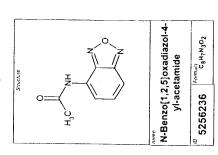


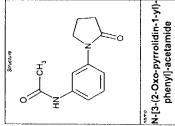


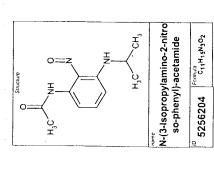


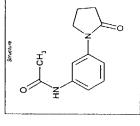


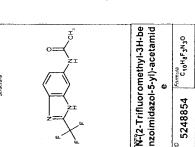


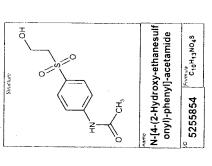


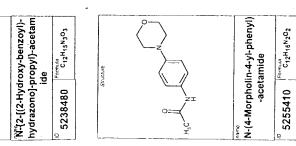








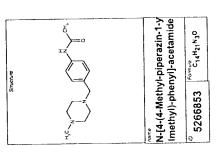


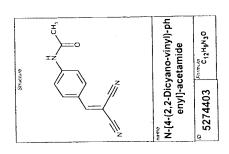


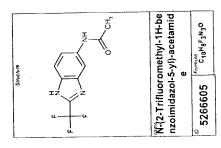
5249307 Formula C12H14N2O2

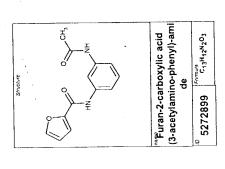


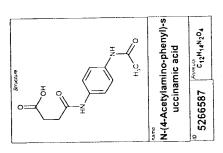


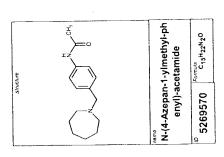


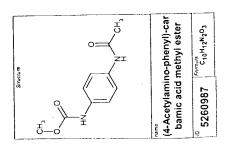












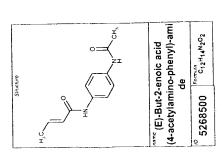
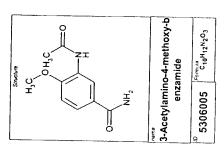
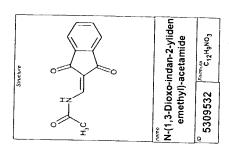


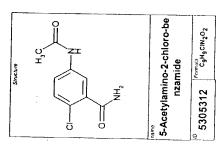
TABLE 15 - 14

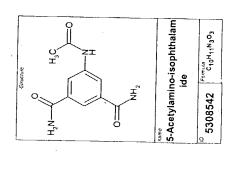


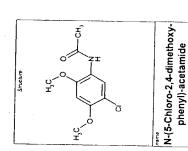










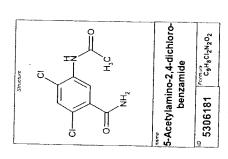


C10H12CINO3

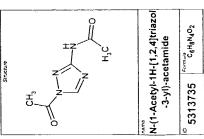
5302797

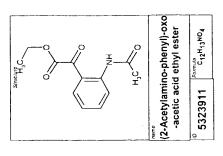
Formula C13H18N2O2

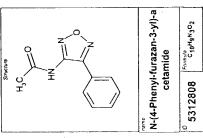
5279673

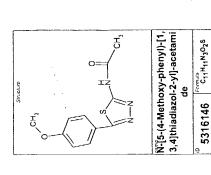




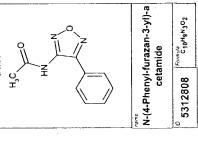






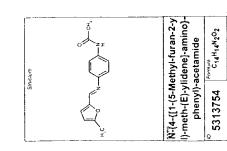


5316146



CH ₃	Z OH	N OH,			N-(8-Methoxy-2,3-dimethyl-quinoxalin-5-yl)-acetamide	C13H15N3O2
~ O-	- €	<u>}</u>	O I)	N-(8-Methoxy quinoxalin-5-	5316088

Sincture	HZ HZ	nane N-(4-Amino-2-methoxy-5-m ethyl-phenyl)-acetamide	Formula C10H14N2O2
Sirvi	N. I.	N-(4-Amino-2. ethyl-pheny	5311167

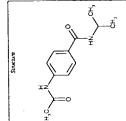


	O +**	in 4 °	4	
	£ F	(2-Methoxy-5-methyl-4 tro-phenyl)-acetamide	Formula C10H12N2O4	
Structure		thoxy-5- tenyl)-ac	1	
	z=0	name N-(2-Methoxy-5-methyl-4-ni tro-phenyl)-acetamide	5310579	

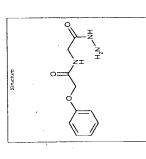


APR 1 4 2003 A	D. H.	N-(4-Oxo-adamantan-1-yl)-a cetamide	5346256 Formula C12H17NO2
		N-(4-0xo	53462

Structure	ZI O H	nano N-(3-Hydroxy-5,7-dimethyl- adamantan-1-yl)-acetamide	Formula C14H23NO2
Sinz	DO. HO	N-(3-Hydroxy adamantan-1-	5352666



NT HO	معسه 4-Acetylamino-N-isopropy benzamide	5334418 Formula 5334418



£ 0	-Chloro-2,5-dimethoxy- phenyl)-acetamide	Formula C ₁₀ H ₁₂ CINO ₃
O I I	N-(4-Chloro-2,5-dimethoxy-phenyl)-acetamide	5331993

Stricture	IZ I

[
	Sinchre	IZ I

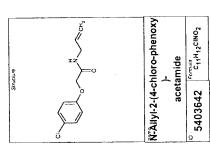
3.3. iide	
ethylene-bicyclo[3.3. .2-en-3-yl)-acetamide	Formula C12H17NO
ethylene 2-en-3-yl	7722

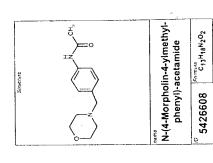
ō >	O D'H	N-(4-Chloro-2,5-dimethoxy-

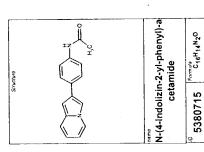
Sinchre	£	N-(6-Methoxy-2-methyl-ben zothiazol-7-yl)-acetamide	FOTH 12N2 025
Sink	Ž-	N-(6-Methoxy zothiazol-7-y	5325303

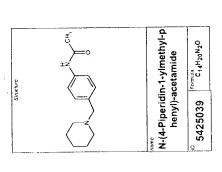


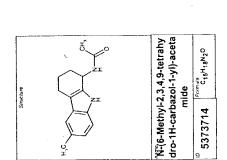


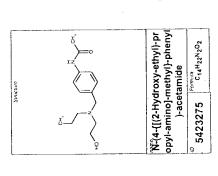


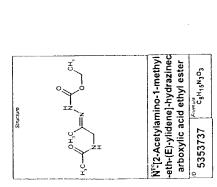


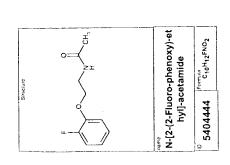










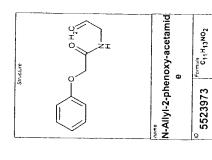


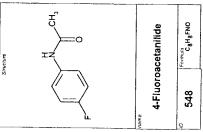


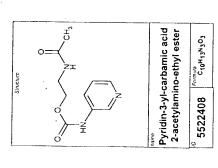
/	OTPE	\
	APR 1 4 2003	
13	ENT.)

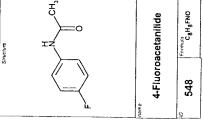
Sincture	H ₃ C CH ₃	N-(4-tert-Butyl-2-nitro-phen vI)-acetamide
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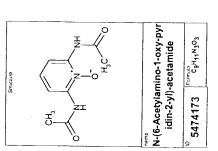
VI O	ռուշ N-(4-tert-Butyl-2-nitro-phen yl)-acetamide	Formula C12H16N2O3
H, C,	N-(4-tert-But)	5485259

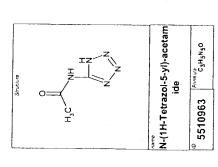


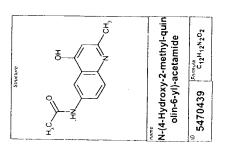












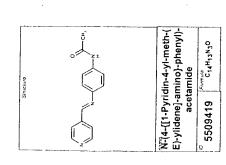
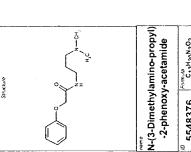
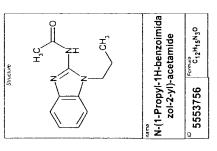


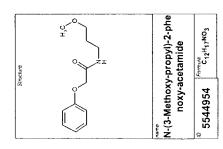
TABLE 15 - 19

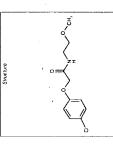


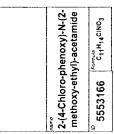


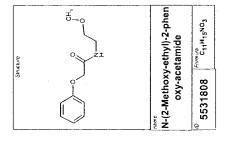
	_	
C13H20N2O2		
5548376		

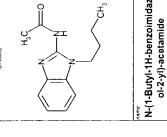




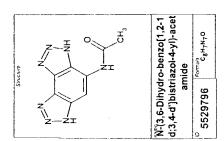


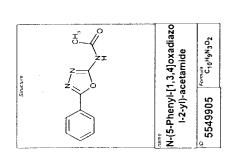






D TH THE THE THE THE THE THE THE THE THE	N-(1-Butyl-1H-benzoimidaz ol-2-yl)-acetamide	5553131 Formula 17N30

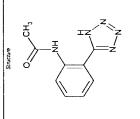




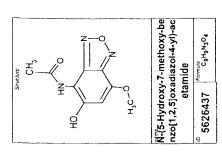


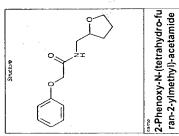






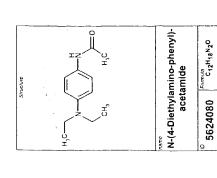
	N-[2-(1H-Tetrazol-5-yl)-phe nyl]-acetamide	Formula CgHgN ₅ O
o'	N-[2-(1H-Tetr nyl]-ac	5583145

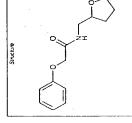


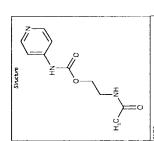


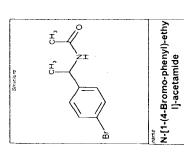
5563979 Formula C13H17NO3

Pyridin-4-yl-carbamic acid 2-acetylamino-ethyl ester 5561171 Formula C10H13N3O3









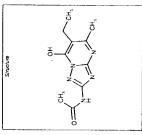
5587422 Formula C10H12BrNO

Sinceture Ch.	N-[1-(3,4-Dichloro-phenyl)-e thyl]-acetamide	10 5583493 Formula C10H11C12NO

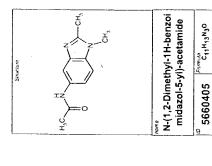
2-Acetylamino-3-benzo[1,3] dioxol-5-yl-acrylic acid Formula C₁₂H₁₁NO₅ 5558887

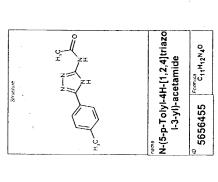


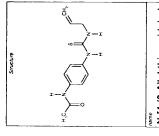


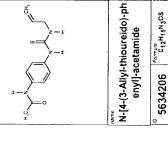


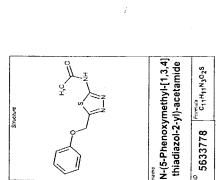
i		
£ × × × × × × × × × × × × × × × × × × ×	N°(6-Ethyl-7-hydroxy-5-met hyl-[1,2,4]triazolo[1,5-a]pyri midin-2-yl)-acetamide	Formula C10H13N5O2
Z Z Z	N-(6-Ethyl-7- hyl-[1,2,4]tria midin-2-yl	5652409

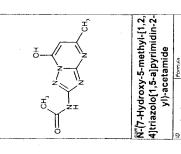


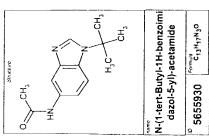








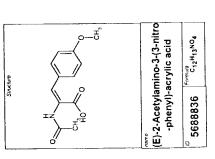


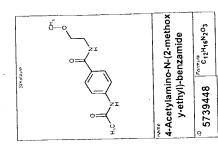












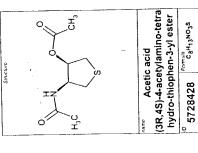


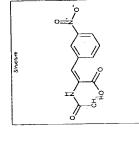
(E)-2-Acetylamino-3-(3-nitro -phenyl)-acrylic acid

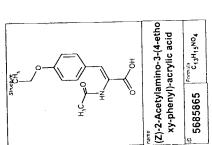
N-[7-0xo-4,5,6,7-tetrahydro-benzothiazol-2-yl]-acetami

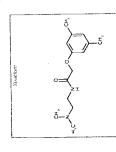
5674030 Formula C9H10N2O2S

5687268 C11H10N2O5









£.	R-2-Dimethylamino-ethyl)- 2-(3,5-dimethyl-phenoxy)-a cetamide	9 Formula C14H22N2O2
	N-(2-Dime 2-(3,5-dim	2690899

5728428

Strature	N-[4-((E)-3-Chloro-but-2-en yloxy)-phenyl]-acetamide	5689801 Framilia 5689801

TABLE 15 - 23

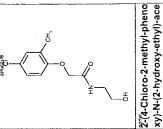








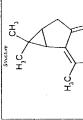




Single on The Chloro-2-me		ф.		thyl-pheno
	elbous	 £ ~	-√	 2-(4-Chloro-2-methyl-pheno



tamide



Sinctine	5 > 2 1	1) (SH
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5798772 Formula C11114CINO3

(4-Acetylamino-benzoylami

no)-acetic acid methyl ester

4-Acetylamino-N-(3-methox y-propyl)-benzamide

Formula C13H18N2O3

5739629

5740840 C12H14N2O4

N-[Acetylamino-(2-chloro-phenyl)-methyl]-acetamide

N-{1-[6,6-Dimethyl-3-oxo-bi cyclo[3.1.0]hex-(2Z)-ylidene]-ethyl}-acetamide

Formula C12H17NO2

5827999

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5811720 C14H15NO3

Structure	0=<
	Š

N-(2-Hydroxy-ethyl)-2-(nap hthalen-1-yloxy)-acetamide

Z, Z	N-(5-Acetyl-2,6-dimethyl-py rimidiņ-4-yl)-acetamide	Fpmuda C10H13N3O2
o Zi	N-(5-Acetyl-2, rimidiņ-4-yl	5810733

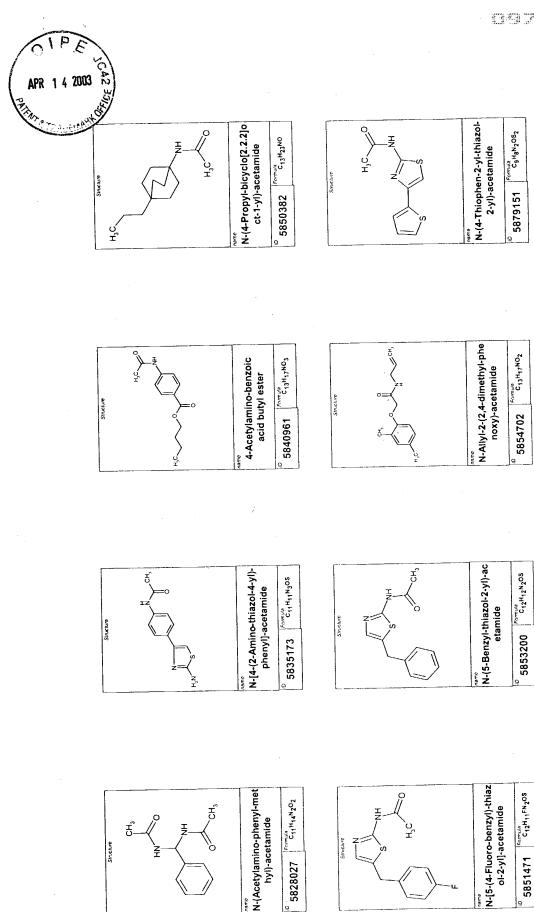
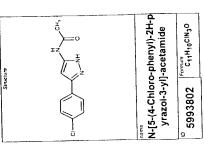
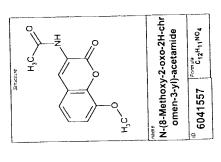
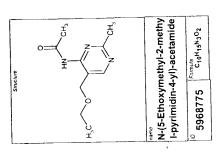


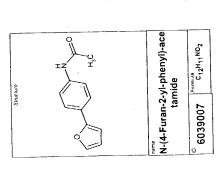
TABLE 15 - 25

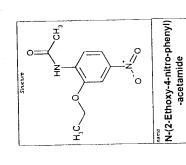




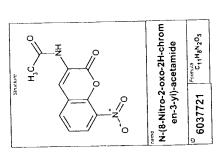






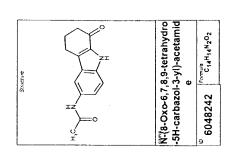


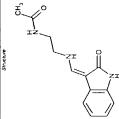
5940353 C10H12N204



Sinclure	T O O O O O O O O O O O O O O O O O O O	N-(6-Methyl-2-oxo-2H-chro men-3-yl)-acetamide	6037500 Formula C12H11NO3







N-(6-Chloro-2-oxo-2H-chro men-3-yl)-acetamide

6041848 C11HaCINO3

C14H13NO3

6041610

6048040 Formula C14H19NO2

N-(8-Allyl-2-oxo-2H-chrome n-3-yl)-acetamide

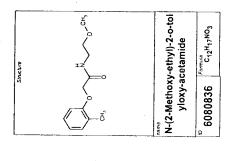
N-Allyl-2-(4-isopropyl-phen oxy)-acetamide Formula C14H19NO2 6047729

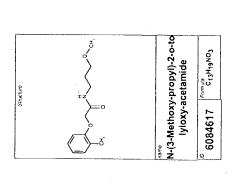
- 27 TABLE 15

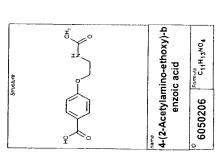


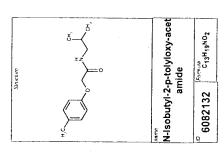
Sincture	IZ	N-(Tetrahydro-furan-2-ylme thyl)-2-o-tolyloxy-acetamid e	Formula C14H19NO3
is.	- P	W-(Tetrahydro thyl)-2-o-toly	6081107

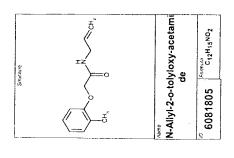
	£	E	
	Š	aceta	15NO2
inre	12	yloxy.	Formula C12H15NO2
Structure		m-toly	1
		ոտո N-Allyl-2-m-tolyloxy-acetam ide	6085276
	υ r	N-A	5









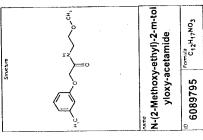


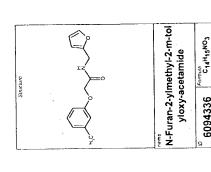




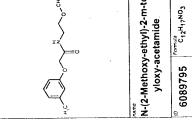
	N-(4-Acetylamino-phenyl)-3 -oxo-butyramide	10 Framula C12H14N2O3

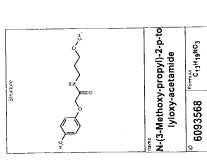
Sincture	\$ \	N-Isobutyl-2-m-tolyloxy-ace	Formula C13H19NO2
S	Š,	N-Isobutyl-2	6095380

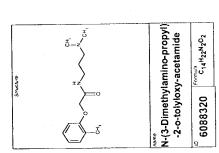




6094336



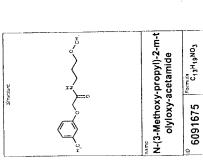




N-(3-Dimethylamino-propyl) -2-m-tolyloxy-acetamide

Formula C14H22N2O2

6085715

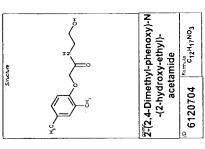


Struct		N-(3-Methoxy lyloxy-a	6093568
	<u></u>	 ± t	

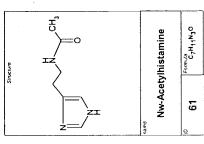
TABLE 15 - 29

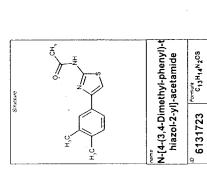


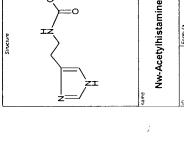


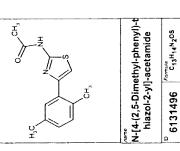


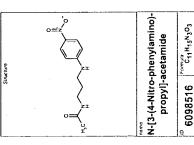
r o	-2-ylo	NO ₂
Sincering	-2-(naphthalen xy)-acetamide	Formula C15H15NO2
š .	N-Allyl-2-(naphthalen-2-ylo xy)-acetamide	6139453
		







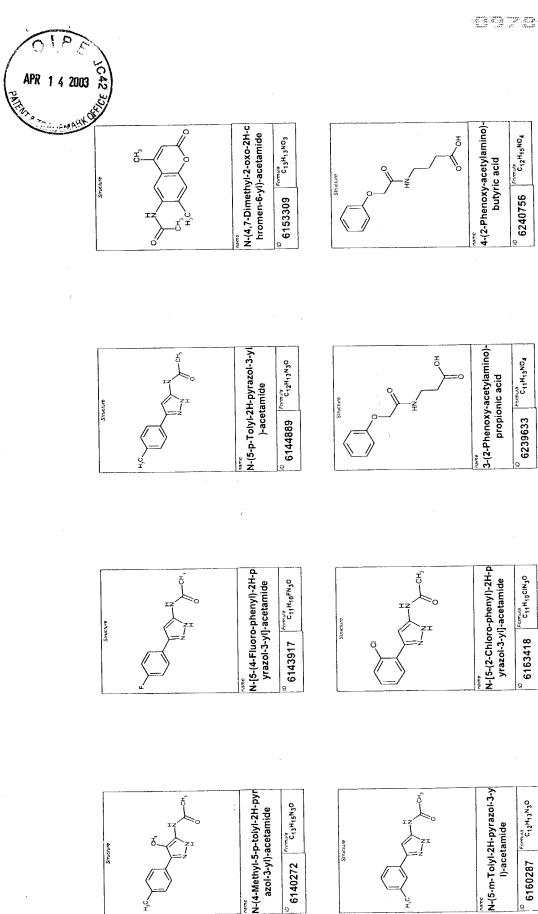




Struchure	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	Note (4-Acetylamino-phenyl)-o xalamic acid ethyl ester	Formula C12H14N2O4
INJS	δ-Zx	N-(4-Acetylam xalamic acid	6127010

2-Phenoxy-N-pyridin-2-ylm ethyl-acetamide	

TABLE 15 - 30



H ₃ C H ₃ C O -5-0xo- ol- 6326			OHO CHO	N-7-1-tert-Butyl-3,4-dimethyl	0-2-yl)-acetamide 0-2-yl)-acetamide 6326390
	ethy!	HN CH ₃ HN CH ₃ Ylamino-(4-dimethyl amide amide amide 6.13 N 19 N 3 O 2		N.C.1-tert	-5-0x0-2,5-1 0l-2-yl) 6326390

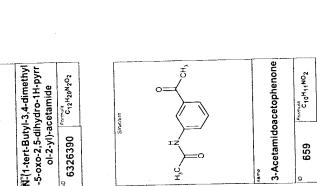
N-(4-Trifluoromethylsulfany I-phenyl)-acetamide

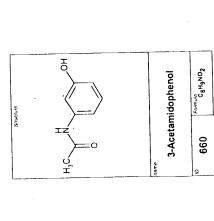
> N-(2-Trifluoromethylsulfany I-phenyl)-acetamide

Formula C9HgF3NOS

6368433

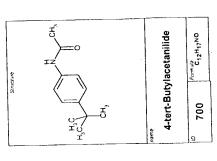
6368862 C9H8F3NOS





N-(5-Methyl-4-p-tolyl-thiazol -2-yl)-acetamide

6404355 Formula 6404355





O D D D D D D D D D D D D D D D D D D D	2-(2-Chloroacetamido)-4-thi azoleacetic acid	6 C7H7CIN2O3S
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